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A combined experimental and computational study of 3-bromo-5-(2,5-difluorophenyl) pyridine and 3,5-bis(naphthalen-1-yl)pyridine: Insight into the synthesis, spectroscopic, single crystal XRD, electronic, nonlinear optical and biological properties

Ghiasuddin [a], Muhammad Akram [a, b], Muhammad Adeel [c, *], Muhammad Khalid [d, e, **], Muhammad Nawaz Tahir [f], Muhammad Usman Khan [g], Muhammad Adnan Asghar [d], Malik Aman Ullah [c], Muhammad Iqbal [c]

[a] Institute of Chemical Sciences, University of Peshawar, Peshawar, KPK, Pakistan
[b] Medicinal Botanic Centre, PCSIR Laboratories Complex Peshawar, KPK, Pakistan
[c] Institute of Chemical Sciences, Gomal University, Dera Ismail Khan, KPK, Pakistan
[d] Department of Chemistry, University of Education Lahore, Faisalabad Campus, Pakistan
[e] Department of Chemistry, Khwaja Fareed University of Engineering & Information Technology, Rahim Yar Khan, Pakistan
[f] Department of Physics, University of Sargodha, Sargodha, Punjab, Pakistan
[g] Department of Applied Chemistry, Government College University, Faisalabad, Pakistan

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ABSTRACT

Carbon-carbon coupling play a vital role in the synthetic field of organic chemistry. Two novel pyridine derivatives: 3-bromo-5-(2,5-difluorophenyl)pyridine (**1**) and 3,5-bis(naphthalen-1-yl)pyridine (**2**) were synthesized *via* carbon-carbon coupling, characterized by XRD, spectroscopic techniques and also investigated by using density functional theory (DFT). XRD data and optimized DFT studies are found to be in good correspondence with each other. The UV–Vis analysis of compounds under study i.e. (**1**) and (**2**) was obtained by using "TD-DFT/B3LYP/6-311 + G(d,p)" level of theory to explain the vertical transitions. Calculated FT-IR and UV–Vis results are found to be in good agreement with experimental FT-IR and UV–Vis findings. Natural bond orbital (NBO) study was performed using B3LYP/6-311 + G(d,p) level to find the most stable molecular structure of the compounds. Frontier molecular orbital (FMO) analysis were performed at B3LYP/6-311 + G(d,p) level of theory, which indicates that the molecules might be bioactive. Moreover, the bioactivity of compounds (**1**) and (**2**) have been confirmed by the experimental activity in terms of zones of inhibition against bacteria and fungus. Chemical reactivity of compounds **(1)** and **(2)** was **in**dicated by mapping molecular electrostatic potential (MEP) over the entire stabilized geometries of the compounds under study. The nonlinear optical properties were computed with B3LYP/6-311 + G(d,p) level of theory which are found greater than the value of urea due to conjugation effect. Two state model has been further employed to explain the nonlinear optical properties of compounds under investigation.

1. Introduction

For synthesis of new compounds; carbon-carbon coupling is having utmost importance. Heck, Stille, Suzuki, Sonogashira and Buchwald-Hartwig reactions have earned much fame in Palladium (Pd) catalysed Carbon-Carbon and Carbon-heteroatom coupling reactions. After advent of Pd catalysis, whole horizon of organic synthesis has changed. During last three decades, Pd catalysis has found its applications in numerous methodologies like

* Corresponding author. Institute of Chemical Sciences, Gomal University, Dera Ismail Khan, KPK, Pakistan.
** Corresponding author. Department of Chemistry, Khwaja Fareed University of Engineering & Information Technology, Rahim Yar Khan, Pakistan..
E-mail addresses: madeel@gu.edu.pk (M. Adeel), khalid@kfueit.edu.pk (M. Khalid).

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regioselective [1], chemoselective [2] and enantioselective [3]. State of the art transition metal catalysts, novel ligand designs and easily accessible reaction conditions have been developed. These transition metal catalysed reaction has found numerous uses in organic synthesis and material synthesis, these reactions also have an important role in pharmaceutical, agrochemical and fine chemical industries [4–8]. Suzuki coupling reaction, developed by Akira Suzuki in 1979 [9], has gained much attention of synthetic community in past 35 years and has become leading reaction in organic synthesis due to quantitative yields of products, use of a variety of substrates/boronic acids combinations, easy availability of catalysts and simplicity of purifications of the products over above mentioned other reactions.

Pyridine is nitrogen containing six membered aromatic heterocyle. It is present in many compounds of natural and synthetic origin and voluminous searches have been carried out on the isolation and synthesis of pyridine and its derivatives [10–13]. Pyridine in addition to being an important member of heterocyclic chemistry has found use as strong base as well as catalyst in many synthetic reactions of medicinal values. The literature about pyridine and its derivatives reveal that a large number of these compounds have been evaluated to have therapeutic prospective against countless diseases [14–17]. Plants are the rich source of pyridine containing compounds. Some of the natural products containing pyridine have been explored exhibiting cancer curative activities [18,19] Number of pyridine derivatives exhibit antifungal activity i.e. 2-Aryl-1,2,4-triazolo[1,5-*a*] pyridine derivatives have shown excellent antifungal activity. N^1-[1-Aryl-2-(1H-imidazol-1-yl and 1H-1,2,4-triazol-1-yl)-ethylidene]-pyridine-2-carboxamidrazone derivatives have shown good antifungal and antimycobaterial activity [20]. Herein, by this research study, we report the synthesis of 3-bromo-5-(2,5-difluorophenyl) pyridine (**1**) and 3,5-bis(naphthalen-1-yl)pyridine (**2**) by employing Pd (0) catalysed Suzuki-Miyaura cross-coupling reaction (Scheme 1). Synthesized compounds (**1**) and (**2**) were characterized by using FT-IR, ^{1}H NMR, ^{13}C NMR, mass spectrometric analysis and single crystal X-ray studies. Both of the synthesized compounds were subjected to density functional theory (DFT) studies to explore more about molecular geometry, frontier molecular orbitals (FMOs), molecular electrostatic potential (MEP), natural bond orbital (NBO) and nonlinear optical (NLO) properties of the synthesized organic structures. This study for the synthesis of compounds **1** and **2** has therefore led us not only to synthesize pyridine derivatives, but also to investigate the structural dynamic of geometries of these molecules. Moreover, compounds (**1**) and (**2**) were subjected to antibacterial and antifungal studies and results of these studies have indicated the potentiality of these compounds as drugs.

2. Experimental

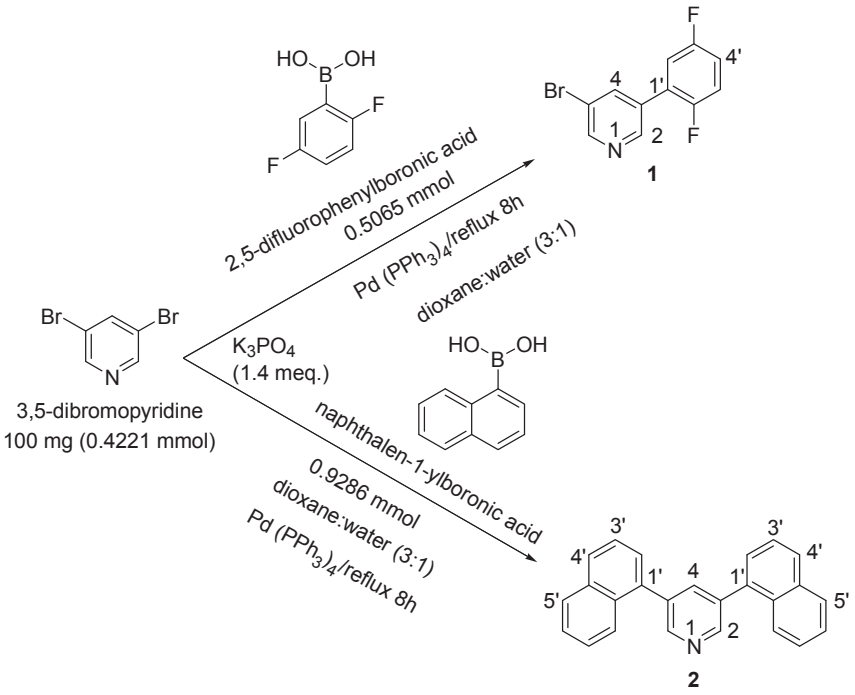
2.1. General experimental

All of the chemicals were used without purification and were purchased from Acros Organics Belgium. Digital melting point apparatus (Stuart, UK) was used to record melting points. FT-IR spectra of the compounds were procured on FT-IR (Shimadzu Prestige, Japan). 400 MHz NMR (Bruker, Switzerland) was used to record ^{1}H and ^{13}C NMR spectra. EIMS and ESI-MS measurements were done on GC-MS (Varian, Japan) and LC-MS (Thermo, USA) respectively. Bruker Smart APEX-II CCD diffractometer was used for single crystal XRD studies.

2.2. Synthesis

2.2.1. Synthesis of 3-bromo-5-(2,5-difluorophenyl)pyridine ***(1)***

To a pressure tube (25 mL) were added 3,5-dibromopyridine (100 mg, 0.422 mmol), 2,5-difluorophenylboronic acid (0.506 mmol), K3PO4 (0.633 mmol), Pd(PhP3)4 (1.5mol%) and dioxane:water (3 mL:1 mL). After flushing with dry nitrogen, pressure tube was sealed with screw-cap, placed in the aluminum container and heated at 90–100 °C for a period of 8 h. After ascertaining the completing of the reaction by TLC, the contents of the pressure tube were extracted thrice with ethyl acetate (3 × 20 mL).



Scheme 1. Scheme for the synthesis of **1** and **2.**